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Running Head: Keratinocyte response to arsenite and UVR *in vitro*

Key Words: arsenite, skin cancer, mouse keratinocyte, solar-simulation UVR, photodamage repair, apoptosis

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Abbreviations: UVR = ultraviolet radiation

CPDs = cyclobutane pyrimidine dimers

6-4PPs = 6-4 photoproducts

TUNEL = terminal deoxynucleotide transferase dUTP nick end labeling

NER = nucleotide excision repair

DPBS = Dulbecco's phosphate-buffered saline

EMEM = Eagle's minimum essential medium

NEAA = non-essential amino acids

FBS = fetal bovine serum

EGF = epidermal growth factor

DMBA=7, 12-dimethylbenz[a]anthracene

ELISA = enzyme-linked immunosorbent assay

OD = optical density

FITC~PBR-1 mAb = FITC-conjugated monoclonal antibody to BrdU

Abstract

Our laboratory has shown that arsenite markedly increased the cancer rate caused by solar-simulation ultraviolet radiation (UVR) in the hairless mouse skin model. The current study investigated how arsenite affected DNA photodamage repair and apoptosis following solar-simulation UVR in the mouse keratinocyte cell-line 291.03C. The keratinocytes were treated with different concentrations of sodium arsenite (0.0, 2.5, 5.0 μM) for 24 h, and then were immediately irradiated with a single dose of 0.30 kJ/m^2 UVR. At 24 h after UVR, DNA photoproducts [cyclobutane pyrimidine dimers (CPDs) and 6-4 photoproducts (6-4PPs)], and apoptosis were measured by using ELISA and two color TUNEL (terminal deoxynucleotide transferase dUTP nick end labeling) assay, respectively. The results showed that arsenite reduced the repair rate of 6-4PPs by about a factor of 2 at 5.0 μM and had no effect at 2.5 μM. UVR-induced apoptosis at 24 h was decreased by 22.64% at 2.5 μM arsenite and by 61.90% at 5.0 μM arsenite. Arsenite decreased the UVR-induced caspase-3/7 activity in parallel with the inhibition of apoptosis. Colony survival assays of the 291.03C cells demonstrate an arsenite LC_{50} of 0.9 μM and a UVR LD_{50} of 0.05 kJ/m^2. If the present results are applicable *in vivo*, inhibition of UVR-induced apoptosis may contribute to arsenite's enhancement of UVR-induced skin carcinogenesis.